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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SINGH, SATYENDRA K	
ART UNIT	PAPER NUMBER
1657	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/764,691	BOWLIN ET AL.	
	Examiner	Art Unit	
	SATYENDRA K. SINGH	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-25* is/are pending in the application.

4a) Of the above claim(s) *3,6-20 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5,21 and 23-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 July 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 06/12/2009 has been entered.

Claims 3, 6-20 and 22 (groups II-VII) remain withdrawn from further consideration. Claim 2 has been previously canceled by applicants.

Claims **1, 4, 5, 21** and **newly added claims 23-25** (group I; as currently amended) are examined on their merits in this office action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1 Claims 1, 4, 5 and 21 (as currently amended) are/remain rejected under 35 U.S.C. 103(a) as being unpatentable over Coffee RA (WO 98/03267; IDS, citation # 70) taken with Coffee RA (US 2001/0003148; IDS, citation # 1) and Coffee RA (US 6,252,129; IDS, citation No. 46), and further in view of Weinberg (US 4,837,379; [A]) .

Claims (as amended) are directed to "**Electrodeposited fibrin matrix with cells**" (or "a construct comprising electrodeposited fibrin matrix with cells"), wherein the cells are delivered to the matrix during fabrication of the electrodeposited fibrin matrix, wherein the cells are suspended in a solution comprising molecules capable of forming fibrin during delivery to the matrix (or wherein the cells are entrapped within the matrix during fabrication of the electrodeposited fibrin matrix, wherein the cells are suspended in a fibrinogen solution during delivery to the matrix, and wherein the cells are oriented through application of mechanical force; wherein the construct has been strained, so that the cells are spread in parallel with the applied force; and wherein the matrix further comprises a cross-linking agent or calcium (see also newly added claims 23-25).

> *"[E]van though **product-by-process** claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).*

Coffee RA (WO 98/03267, IDS) discloses electrohydrodynamically making (taken as a process of electrodeposition; see Coffee RA, pages 9-10, in particular) fiber mats for use **in treating wounds or burns** (see Coffee RA, abstract, and claims I-5, in particular). Among the various fibers that may be used is **fibrin**, which may be formed *in situ* by action of thrombin on fibrinogen (see Coffee RA, page 28, claims 20, 25-26, 36). A wide range of biologically active ingredients may be incorporated, including nucleic acids, growth factors, therapeutic agents, cells, etc. (see Coffee RA, pages 5-6, in particular). The fiber mat may be incorporated into **conventional bandages and wound dressings** (see Coffee RA, pages 6 and 17, in particular), thus the product produced encompasses electrodeposited fibrin matrix with cells. In addition, Coffee RA discloses the fact that the liquid used for electrodeposition may "comprise a solution, suspension, microsuspension, emulsion....which may contain an active components or components (see Coffee RA, page 5, 2nd and 3rd paragraphs, pages 6-7, 22-23 and 28, in particular), which are disclosed as encompassing various pharmaceutical compounds such as drugs, including "biological products such as cells, and cytokines" (see page 5, 3rd paragraph, in particular), wherein the cells may be interspersed in or between layers of the electrodeposited composition (see page 23, 2nd paragraph, in particular).

Coffee RA (US 2001/0003148; IDS) discloses an **electrohydrodynamic method** of producing mats from suitable fibers, which process is reasonably expected to produce electrodeposited matrix with cells. Specifically, fibrin is produced (paragraph 0017, 0085, claim 26 and claim 36). The fibrin fibers may comprise additional biologically active material (paragraph 0021). Coffee RA (US 6,252,129) discloses an electrohydrodynamic method of producing mats from suitable fibers. Specifically, fibrin is produced (column 3, line 43; column 14, line 12). The fibers may comprise additional biologically active material (see, paragraph bridging columns 3-4).

Even though, an electrodeposited fibrin matrix comprising cells is not explicitly exemplified by the referenced inventions of Coffee RA (WO 98/03267; IDS, citation # 70), Coffee RA (US 2001/0003148; IDS, citation # 1), and Coffee RA (US 6,252,129; IDS, citation No. 46), this product is clearly envisioned by the reference disclosures.

Given the fact that Coffee RA (WO 98/03267, IDS) discloses that a product as claimed, i.e. an electrodeposited fibrin matrix is made using solutions or suspensions comprising **fibrinogen and/or thrombin** (see claims 15-20, 26, 36-38, in particular), wherein the solutions or liquids can be further added with **polymers or cells and/or other biological components** such as growth factors, drugs, peptides, etc (see Coffee RA, discussion above), and electrodeposited on a desired surface to produce a fibrin **mat or web** (i.e. fibrin matrix) which can be interspersed with the cells between the layers (see Coffee RA, page 23, 2nd paragraph, in particular), it would have been clearly obvious to a person of ordinary skill in the tissue engineering art to incorporate cells (such as skin cells) and/or other biological components (such as drugs, hormones, peptides, etc.) in the fibrin matrix in order to provide an electrodeposited fibrin matrix with cells having the benefits of incorporated biological agents such as drugs, for example in the form of a superior **wound dressing or covering, or skin substitute**, as exemplified by Coffee RA, WO 98/03267; see abstract, pages 4-7, pages 17-19, pages 22-23 and 28; and claims, in particular.

However, a product as claimed in newly presented claim 24, i.e. an electrodeposited fibrin matrix with cells further comprising **a cross-linking agent**, though implicitly suggested (see Coffee WO 98/03267; page 17, last paragraph, in particular for creating a product in the form of a network of crossing or interlinking fibers to result in web or mat), is not explicitly taught by the cited prior art references (Coffee RA, as discussed above).

Weinberg [A] discloses use of **cross-linking agents** in the process of making fibrin-collagen tissue equivalents that also comprise cells (see Weinberg, abstract, summary of the invention, column 4, 1st paragraph, columns 5-7, and claims, in particular), wherein the cross-linking agent such as Factor XIII is used (see column 7, 2nd paragraph and example 2, in particular) to provide strength to the fibrin-collagen tissue equivalents by cross-linking or chemically stabilizing fibrin and collagen (a structural protein ubiquitously present in and around mammalian cells and tissues)

lattice that contains mammalian cells such as fibroblast cells (see column 6, in particular).

Thus, it would have been obvious to a person of ordinary skill in the clinical art (at the time this invention was made) to include a cross-linking agent (as explicitly taught by Weinberg [A]) in the process as disclosed by Coffee RA (see discussion above) to achieve a better and tougher electrodeposited fibrin matrix containing cells, the benefit which is desired and explicitly disclosed by Weinberg et al (see column 6, in particular). An artisan of ordinary skill in the clinical art would be motivated, and would have had a reasonable expectation of success in including a cross-linking agent that is added to the product disclosed by Coffee RA, as Weinberg clearly discloses the benefits associated with the addition of such cross-linking agents as factor XIII (i.e. for achieving superior strength of the tissue equivalents comprising fibrin).

The process limitations as recited in instant claims, wherein the cells are delivered to the matrix during fabrication of the electrodeposited fibrin matrix, wherein the cells are suspended in a solution comprising molecules capable of forming fibrin during delivery to the matrix, or wherein the cells are entrapped within the matrix during fabrication of the electrodeposited fibrin matrix, wherein the cells are suspended in a fibrinogen solution during delivery to the matrix (see instant claims 1, and 21), are disclosed by Coffee RA, as it describes the same process steps of electrodeposition of materials in liquid, solution or suspension form (containing polymers, and/or cells and other beneficial biological components such as drugs, hormones, etc.) in order to obtain the electrodeposited fibrin matrix or mat containing cells. In the absence of any evidence to contrary, the “electrodeposited fibrin matrix with cells” product as explicitly suggested by the referenced invention of Coffee RA (WO 98/03267, US 2001/0003148), and US 6,252,129 is deemed to be substantially similar if not the same as the claimed product. In addition, the inclusion of a cross-linking agent in order to provide strength (by cross-linking fibrin and collagen fibers) to the product obtained (i.e. the electrodeposited fibrin matrix containing cells as discussed above) would have been an obvious step in the process of making such tissue equivalents or products, as disclosed by Coffee RA, in view of the disclosure provided by the cited prior art reference of Weinberg.

The limitations of orienting cells through mechanical force, or “wherein the construct has been strained, so that the cells are spread in parallel with the applied force" have been explicitly or implicitly taught by the process disclosed by the referenced invention of Coffee (WO 98/03267, IDS) as discussed above, and would have been fully contemplated by an artisan of ordinary skill in the art at the time the claimed invention was made. Moreover, such process limitations are deemed to be intrinsic to the process of making the matrix material containing fibrinogen and cells as taught and/or suggested by the combined teachings of the cited references of record.

The limitations of the matrix further comprising **calcium** is met by the cited prior art reference of Weinberg [A] that discloses the fact that calcium ions are necessary for the formation of fibrin from fibrinogen in the presence of thrombin (see column 6, first and last paragraphs, in particular), and can be conveniently provided in various forms or at various steps in the process, as per need or suitability. Thus, an artisan of ordinary

skill in the clinical and tissue regeneration art would be motivated to use calcium in the presence of thrombin (or an analog thereof) in order to stabilize (as fibrin is known to clot in the presence of the calcium ion; see Weinberg, column 6, lines 6-9, in particular) the electrodeposited fibrin matrix containing cells, the fabrication of which is explicitly suggested by Coffee.

Thus, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill in the tissue engineering or clinical art at the time the claimed invention was made.

As per MPEP 2111.01, during examination, the claims must be interpreted as broadly as their terms reasonably allow. In re American Academy of Science Tech Center, F.3d, 2004 WL 1067528 (Fed. Cir. May 13, 2004)(The USPTO uses a different standard for construing claims than that used by district courts; during examination the USPTO must give claims their broadest reasonable interpretation.). This means that the words of the claim must be given their plain meaning unless applicant has provided a clear definition in the specification. In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).

As per MPEP 2144.06, "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

As per MPEP 2144.04, Ex parte Rubin, 128 USPQ 440 (Bd. App. 1959) (Prior art reference disclosing a process of making a laminated sheet wherein a base sheet is first coated with a metallic film and thereafter impregnated with a thermosetting material was held to render prima facie obvious claims directed to a process of making a laminated sheet by reversing the order of the prior art process steps.). See also In re Burhans, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results); In re Gibson, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.).

Response to Applicant's Arguments

Applicant's arguments filed with the office on 06/12/2009 (see response, pages 6, in particular) with respect to claims 1, 4, 5, 21 and newly added claims 23-25 (as they pertain to the prior art rejections of record) have been considered but are not found to be persuasive for the following reasons of record:

Applicants argue the following:

"As amended, independent claim 1 from which claims 4 and 5 depend and 21 require that the mechanical force be applied to orient the cells of the electrodeposited fibrin matrix. None of the cited references, each alone or in any

combination teach or suggest the instant claimed subject matter. Accordingly, Applicants respectfully request that the rejection be withdrawn."

In response, it is noted that the obviousness rejection of record as discussed above teaches and/or suggests all the limitations as currently presented in the claims 1, 4, 5, 21, and 23-25. The limitations of orienting cells through mechanical force, or "wherein the construct has been strained, so that the cells are spread in parallel with the applied force" have been explicitly or implicitly taught by the process disclosed by the referenced inventions of Coffee (WO 98/03267, IDS) as discussed above. Such process limitations are deemed to be intrinsic to the process of making the matrix material taught by the cited references of record. The inclusion of calcium in the solution for electroprocessing to form the fibrin matrix or construct comprising such matrix with cells would have been obvious to a person of ordinary skill in the art as calcium is necessary for the formation of fibrin from fibrinogen solution as explicitly disclosed by the referenced invention of Weinberg (see column 6, last paragraph, in particular). Similarly, the inclusion of a cross-linking agent in such fibrin containing composition have been suggested by the disclosure of Weinberg, as discussed above in the obviousness rejection of record. Thus, the 103a rejection of record has been properly made & maintained.

Conclusion

NO claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SATYENDRA K. SINGH whose telephone number is (571)272-8790. The examiner can normally be reached on 9-5MF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sandra Saucier/
Primary Examiner, Art Unit 1651

/Satyendra K. Singh/
Examiner, Art Unit 1657